Thromboembolic Disease: PBL

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- Prothrombin complex concentrate (PCC)

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Dr. Tambunan is a frequent and popular FMX presenter. He practices internal medicine and has been teaching for 20 years. He specializes in anticoagulation, venous thromboembolism, and viral hepatitis.

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Learning Objectives

1. Practice applying new knowledge and skills gained from Thromboembolic Disease sessions, through collaborative learning with peers and expert faculty.
2. Identify strategies that foster optimal management of thromboembolic diseases, within the context of professional practice.
3. Formulate an action plan to implement practice changes, aimed at improving patient care.

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Associated Session

- Pulmonary Embolus & Deep Vein Thrombosis: The New Frontier

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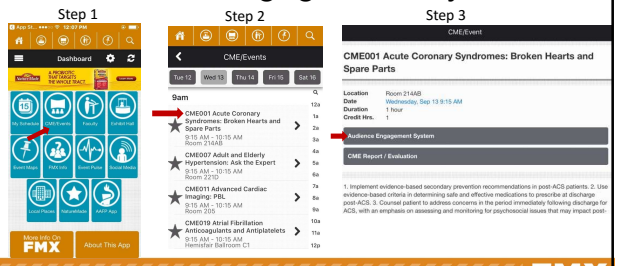
Audience Engagement System



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Chief Complaint

- Left leg pain

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History of Present Illness

- SD, 65 year old woman comes in with acute shortness of breath for the last 2-3 days. She just returned from visiting her daughter in Indonesia last week. Pt also noticed that her left leg was more swollen than usual. Denies any cough, fever, or vomiting or coughing of blood.

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PMH

- DM type 2 for 10 years
- Hypercholesterolemia

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FH

- Mother: Diabetes, Hypertension, Breast CA
- Father: Hypertension
- Sibling: Sister has breast cancer

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Medications

- Metformin 1000 mg BID
- Lisinopril 2.5 mg Qday
- Estrogen 0.625 mg ½ tab Qday
- Atorvastatin 40 mg Qday

- Allergy: NKDA

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Immunizations

- MMR as a child
- Td – 7 years ago
- Pneumoniae vaccine up to date

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Social History

- Tobacco – Denies
- EtOH - Denies
- IVDA – Denies
- Occupation – retired. Previously an accountant

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Review of Systems

- Gen: More easily fatigued
- Resp: Shortness of breath
- GI: Intermittent nausea feeling
- MSK: Leg pain on the left

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Physical Examination

- Vitals: B/P 122/74, HR – 115, O2 sat = 91% on RA
- Neck: JVD – normal
- Heart: Tachycardic but regular with no murmur or gallop or rub
- Lung: CTAB
- Abd: Soft, NT, NABS, no HSM
- Ext: good pulse, mild asymmetry in leg size L>R, no peripheral edema

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Laboratory/Radiology

- Na = 136, K = 4.1, Cl = 104, HCO3 = 22, BUN = 24, Creat = 1.1, Gluc = 99, ALT/AST = 48/58, Alb 3.5, Bili = 0.8
- WBC 9.9, Hgb 12.9, Hct = 38, Plt = 333
- EKG shows sinus tachycardia, T wave inversion on V 1-4
- CXR: Normal

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AES POLL QUESTION

- What is the patient's Well Score?
  - A. 1
  - B. 2
  - C. 4
  - D. 5
  - E. 7.5

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Pretest Probability of PE

Clinical signs and symptoms of DVT	3 points
An alternative diagnosis is less likely than PE	3 points
Heart rate > 100	1.5 points
Immobilization or surgery in previous 4 weeks	1.5 points
Previous DVT/PE	1.5 points
Hemoptysis	1 point
Malignancy	1 point

Low – Less than 2 points → 3% probability
Moderate -- 2 – 6 points → 28%
High -- > 6 points → 78%

Wells PS, et al. Thromb Haemost 2000;83:416-20.

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AES POLL QUESTION

- What test (s) would you order?
  - A. D-dimer ELISA
  - B. Doppler ultrasound
  - C. CT angiogram of the chest
  - D. Pulmonary angiogram
  - E. B and C

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AES POLL QUESTION

- What would your next management step if the Doppler ultrasound of the left leg and the CTA are positive?
  - A. Send home and start patient on a NOAC
  - B. Admit and start unfractionated heparin & warfarin
  - C. Admit and start low molecular weight heparin
  - D. Admit and consult the vascular surgeon for thrombolytics

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AES POLL QUESITON

- What is your oral anticoagulation choice?
  - A. Warfarin
  - B. Apixaban
  - C. Dabigatran
  - D. Edoxaban
  - E. Rivaroxaban

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	Dabigatran	Apixaban	Rivaroxaban	Edoxaban
Indications	Nonvalvular a. fib. DVT & PE treatment DVT prophylaxis	Nonvalvular a. fib. DVT & PE treatment DVT prophylaxis	Nonvalvular a. fib. DVT & PE treatment DVT prophylaxis	Nonvalvular a. fib. DVT & PE treatment
Mechanism of action	Thrombin inhibitor	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
Administration route	Oral	Oral	Oral	Oral
Clearance	Renal	Renal & Hepatic	Renal & Hepatic	Renal & Hepatic
Dosage	150 mg BID	5 mg BID	20 mg QDay	60 mg QDay
Antidote	None	?PCC	?PCC	? PCC
Pregnancy	C	B	C	C
Severe drug interactions	**Azoles, amiadarone**, rifampin, anticonvulsants	**Azoles, diltiazem**, rifampin, anticonvulsants	**Azoles, HIV protease inh, quinidine**	**Verapamil, Quinidine**, rifampin, anticonvulsants
Dose adjustments	CrCl 30-50 – 75 mg BID CrCl < 30 -- **NO**	If + on 2 out of 3: 1. Age > 80 yrs old 2. Body weight <60 kg 3. Creat > 1.5 mg/dL Reduce dose to 2.5 mg BID	CrCl 15-50 – 15 mg daily CrCl < 15 - **NO**	CrCl > 95 – **NO** CrCl 15-10 – 30 mg daily

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Switching anticoagulants

Agents	Recommendations
VKA to NOAC	INR <2.0: immediate INR 2.0-2.5: immediate or next day INR >2.5: follow INR till <2.5
NOAC to VKA	Administer concomitantly until INR is appropriate Re-test 24 hr after last dose of NOAC
Parenteral to NOAC: UFH LMWH	 Start once UFH is discontinued. Caution: Renal Start when next dose would be given
NOAC to parenteral	Initiate when next dose of NOAC is due

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Assesment

- Pt was admitted and was placed on UFH drip. CTA shows multiple clots at the secondary branches of the pulmonary artery and positive Doppler ultrasound on the left popliteal vein. After five days of hospitalization, pt was noted to have epistaxis and platelet count of 80,000 with stable Hgb.

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AES POLL QUESTION

- What is the cause of the drop in platelets in the patient?
  - A. Lab error
  - B. Citrate induced thrombocytopenia
  - C. Heparin induced thrombocytopenia
  - D. Massive internal bleeding

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Heparin Induced Thrombocytopenia (HIT)

- Definition: + heparin antibody with fall of platelets (> 50%) or skin lesions at injection site or systemic reactions post heparin infusion
- Bovine UFH > porcine UFH > LMWH
- Recommend to monitor platelets every-other-day between days 4 – 14 (especially in postoperative patients)
- **DO NOT** use warfarin solely in HIT-associated DVT – may cause venous limb gangrene

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Direct Thrombin Inhibitor

- Identical to the natural hirudin found in leeches
- Cleared thru the kidney, adjust as needed
- Two agents: Argatroban and Lepirudin
- Lepirudin: Two prospective studies involving 380 pts, showing >90% platelet recovery and >75% effective anticoagulation. In addition, the difference in cumultative risk of death, limb amputation, or new thromboembolic complications are statistically significant in favor of lepirudine, p <0.004
  - Dosage: 0.4 mg/kg (max 110 kg) bolus, then 0.15 mg/kg (max 110 kg)
- Other agent is argatroban 2 mcg/kg/min IV to maintain aPTT 1.5-3 times baseline

Greinacher A, Lubenow N. Circulation. 2001;103:1479-1484.

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Which anticoagulant?

- Cancer
- Poor compliance
- Pregnancy
- Reversal agent needed
- Liver disease
- Renal disease & CrCl < 30 mL/min

- LMWH
- VKA
- LMWH
- VKA, UFH, Dabigatran
- LMWH
- VKA

Kearon C, Alk E, et al. Chest 2016;149:315-352

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Other management options

- Inferior Venal Caval Filter
  - contraindication or complication from anticoagulant therapy
  - recurrent thromboembolism despite adequate anticoagulation
  - chronic recurrent embolism with pulmonary hypertension
  - concurrent performance of surgical pulmonary embolectomy
- Thrombolytic Therapy
- Surgical Pulmonary Embolectomy
- Catheter Transvenous Extraction

Kearon C, Kahn SR, et al. Chest 2008;133:454S-545S

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Patient Education and Follow up

- Take prescribed medications as directed
- Watch how much vitamin K intake (warfarin)
- Be on the look for excessive bleeding/bruising
- Wear compression stockings
- Avoid sitting still
- Make lifestyle changes
- Get regular exercises
- Check in with your doctor regularly

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Questions

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